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P3092 Indirect evidence for free radical release following exercise-induced ischaemia resulting in myocardial stunning

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Direct and indirect evidence suggests that oxygen derived free radicals play a pathogenetic role in myocardial stunning. We investigated whether exercise-induced myocardial stunning was associated with free radical release in man.

Methods: 10 men (aged 59 ± 9 years) with triple vessel coronary artery disease, stable angina and normal left ventricular function performed symptom-limited treadmill exercise tests. Serial transthoracic echocardiography (ECHO) was performed before, and at regular intervals after exercise. Peripheral venous blood samples were taken prior to and immediately after exercise, and assays of lipid peroxidation were performed using HPLC as an indirect measure of free radical generation and resultant peroxidation.

Results: Heart rate, blood pressure and ST changes returned to baseline within 10 minutes of exercise in all patients. Exercise duration was 394 ± 180 secs, and maximum ST depression was 1.9 ± 1 mm. Quantitative ECHO data (mean \pm SD) pre exercise, 30 minutes and 240 minutes post exercise are shown:

	Pre exercise	30' post	240' post
IRP (msecs)	90 ± 9	$106 \pm 11^*$	90 ± 8
EF(%)	59 ± 8	$52 \pm 10^*$	59 ± 7
SF(%)	3.8 ± 0.9	$1.8 \pm 0.8^*$	3.6 ± 1.1

*p < 0.001 vs pre exercise

[IRP = isovolumic relaxation period, SF = shortening fraction in the ischaemic region, EF = global ejection fraction]

Significant systolic and diastolic abnormalities are demonstrated at 30 minutes post exercise due to myocardial stunning.

Markers of lipid peroxidation are shown below (mean \pm SEM).

	Pre exercise	Post exercise
Malondialdehyde (MDA) ($\mu\text{mol/l}$)	0.61 ± 0.06	1.08 ± 0.11 (p < 0.01)
Lipid hydroperoxides ($\mu\text{mol/l}$)	1.13 ± 0.06	1.43 ± 0.08 (p = 0.12)

A significant rise in MDA a marker of lipid peroxidation was detected following ischaemia, lipid hydroperoxides also rose but not significantly.

In conclusion, our finding of increased lipid peroxidation following ischaemia is consistent with the hypothesis that oxygen radicals play a pathogenetic role in myocardial stunning in humans.

P3093 Different epicardial and endocardial activation of K_{ATP} channels might cause peaked T-waves during acute coronary occlusion

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Purpose: We tested a hypothesis that there is a difference in epicardial (Epi) and endocardial (Endo) activation of K_{ATP} channels, which might cause electrocardiographic ST-T changes.

Methods: In anaesthetized open-chest dogs, a sequence of 5-min occlusion and 30-min reperfusion of the left anterior descending coronary artery was repeated, while Epi and Endo monophasic action potentials (MAPs) were recorded from the centre of ischaemic zone (n = 14). In a separate group (n = 7), unipolar electrograms were recorded from 47 Epi sites within the ischaemic zone using a mapping system. 5-hydroxydecanoate (30 mg/kg; 5-HD) or glibenclamide (0.25 mg/kg; GLB), specific blockers of K_{ATP} channels, or nicorandil (0.25 mg/kg; NCR), an opener, was administered intravenously before the third or fourth occlusion, then the data were compared with the second (control) occlusion data. Heart rate was kept constant by atrial pacing.

Results: During control occlusion, shortening rate of MAP duration at 90% repolarization was greater at Epi than Endo layer ($19.7\% \pm 1.5$ vs. $13.1 \pm 2.4\%$, mean \pm SE, n = 14, p < 0.05). 5-HD suppressed the shortening rate preferentially at Epi layer, and reduced the difference between the two layers (11.0 ± 3.5 vs. $11.5 \pm 3.7\%$, n = 6, NS). In contrast, NCR augmented the shortening preferentially at Epi layer, and increased the difference (29.0 ± 2.0 vs. $5.9 \pm 3.0\%$, n = 6, p < 0.05). Concordantly, occlusion-induced increase in the peak amplitude of T-waves was suppressed by GLB while augmented by NCR (control occlusion: 10.5 ± 0.5 , GLB: 5.6 ± 0.4 , NCR: 12.8 ± 0.5 mV, n = 7, p < 0.05). Collateral blood flow measured using radioactive microspheres during control occlusion was greater at Epi than Endo layer (31.3 ± 12.5 vs. 8.9 ± 3.1 ml/100 g/min, n = 8, p < 0.05).

Conclusion: These data suggest that epicardially dominant activation of K_{ATP} channels despite less severe ischaemia increases the time lag between Epi and Endo repolarization, thereby contributing to the formation of electrocardiographic, peaked T-waves immediately after acute coronary occlusion.

THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION

P3094 Powerful antioxidant fails to improve left ventricular function after thrombolytic therapy in patients with acute myocardial infarction

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Histochrome (H) – water-soluble form of 2, 3, 5, 6, 8-pentahydroxyl-7-ethyl-1, 4-naphthoquinone possess high cardioprotective activity in the animal models of coronary occlusion/reperfusion. We investigated the effect of H. treatment during thrombolytic therapy (TLT) in patients with acute myocardial infarction (AMI) on global and regional left ventricular (LV) function. 18 pts (17 men) with successful thrombolysis (intravenous- i.v. and/or intracoronary-i.c.) in a first anterior Q-wave AMI were included in the final analyses of the pilot study. Study design: randomised, opened. There were equal number pts in each group (9 in control-C. and H. group). No statistically significant differences were noted in the mean age (53.0 ± 3.9 y in C. vs. 54.6 ± 2.9 y in H., p = NS) in the time from pain to TLT (2.91 ± 0.58 h C. vs. 3.0 ± 0.44 h H., p = NS) in the time from pain to peak creatine kinase (CK) activity (10.90 ± 1.21 h vs. 13.80 ± 1.62 h, respectively; p = NS) and adjunctive drug regimen between groups. The dosage schedule included 100 mg bolus injected i.v. just before TLT and 100 mg bolus 1 hour later. All pts underwent echocardiography on 1–2 d and 14–21 d for LV function assessment. Wall motion analysis was done within the frame of the 16-segment model. We calculated global wall motion index (WMI), regional (infarct-related) wall motion index (RWMI), end-diastolic and end-systolic volume indexes (EDVI, ESVI ml/m²), ejection fraction (EF%). Serial blood samples for measuring CK plasma level were taken.

Results.

Group	Histochrome	Control	p	Group	Histochrome	Control	p
EDVI 1–2 d	65.1 ± 7.1	61.8 ± 6.0	NS	WMI 1–2 d	1.70 ± 0.14	1.88 ± 0.08	NS
EDVI 14–21 d	80.2 ± 8.1	74.0 ± 7.1	NS	WMI 14–21 d	1.54 ± 0.12	1.75 ± 0.09	NS
ESVI 1–2 d	39.0 ± 5.9	42.2 ± 3.9	NS	RWMI 1–2 d	2.48 ± 0.10	2.78 ± 0.12	NS
ESVI 14–21 d	47.2 ± 5.2	43.8 ± 4.5	NS	RWMI 14–21	2.30 ± 0.19	2.63 ± 0.15	NS
EF 1–2 d	41.2 ± 4.3	31.2 ± 3.9	NS				
EF 14–21 d	40.5 ± 3.8	40.4 ± 4.3	NS				

Non-significant difference between groups were observed in peak CK (2941 ± 577 U/l in H. vs. 3730 ± 770 U/l in C.; p = NS).

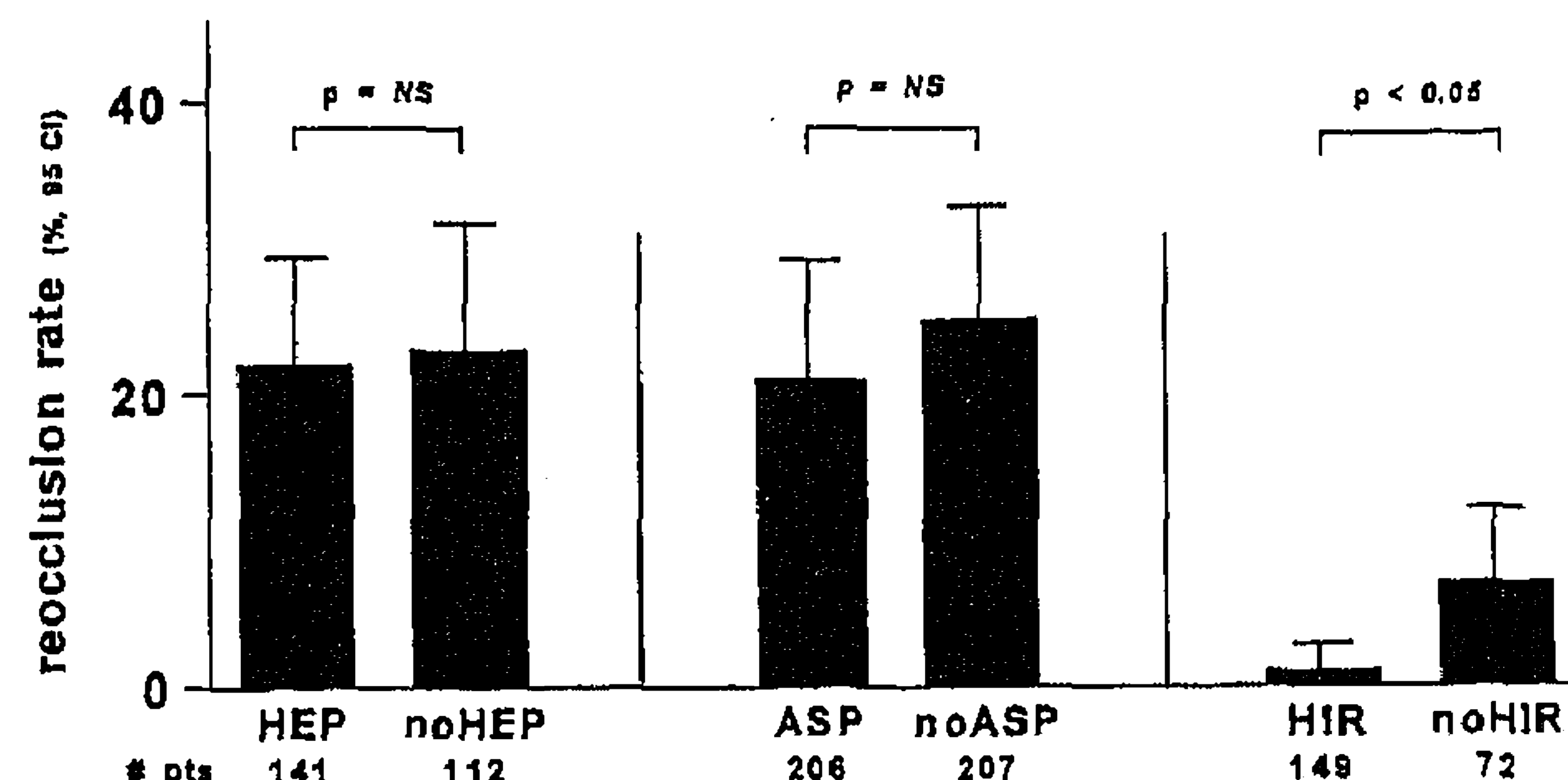
Conclusion: H. had no significant effect on LV global and regional function after successful thrombolysis in pts with anterior Q-wave AMI in our pilot study.

P3095 Hirudin and hirulog, but not heparin or aspirin seem to prevent reocclusion following successful thrombolysis

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Both heparin (HEP) and aspirin (ASP) apart or combined lead to better outcome in patients (pts) with acute myocardial infarction (AMI) undergoing thrombolytic therapy (TT), supposedly due to prevention of reocclusion.

In numerous trials in pts treated with TT for AMI both HEP and ASP apart and combined have shown to improve patency of the infarct-related vessel (IRV) by angiography 90 minutes to several days after TT. But this does not prove that HEP or ASP prevents reocclusion. For the diagnosis of true reocclusion 2 angios are needed: one with an open IRV and one follow-up angio. There are 7 published angiographic trials fulfilling these criteria, which directly compare HEP (n = 2), ASP (n = 3) or hirudin/hirulog (HIR, n = 2) to reference therapy.



Thus, both heparin and aspirin apart and combined improve IRV patency by facilitating thrombolysis rather than preventing reocclusion after TT for AMI. Only hirudin and hirulog seem to prevent re-occlusion after successful TT.